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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,555	11/15/2001	Gregory Paul Dittmar	8341	2834

27752 7590 09/23/2003

THE PROCTER & GAMBLE COMPANY
INTELLECTUAL PROPERTY DIVISION
WINTON HILL TECHNICAL CENTER - BOX 161
6110 CENTER HILL AVENUE
CINCINNATI, OH 45224

EXAMINER
FUBARA, BLESSING M

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 09/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/996,555	DITTMAR ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Examiner acknowledges receipt for extension of time and amendment A filed 07/14/03.

Claim Rejections - 35 USC § 112

1. The rejection of claims 1-24 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of the amendments to the claims.

Claim Objections

2. The objection to claims 8, 10, 19 and 21 is withdrawn because the claims have been amended.

Claim Rejections - 35 USC § 102

3. Claims 1-4, 8-14 and 19-22 remain rejected under 35 U.S.C. 102(b) as being anticipated by Iamartino et al. (US 5,171,580, cited by applicants on form PTO 1449).

Applicants argue that applying the outer coating directly on the inner layer excludes the intermediate layer of the Iamartino reference.

4. Applicants' arguments filed 07/14/03 have been fully considered but they are not persuasive. The comprising language of the generic claims does not exclude Iamartino as a reference. The rejection is reiterated below:

Iamartino discloses an oral pharmaceutical preparation that comprises a core of active ingredient coated with three protective layers (abstract, column 3, lines 15-20). Iamartino states that coating the core of therapeutically active agents with the three layers allows specific and reliable release of the active substance directed to the lower part of the intestine and especially to the large intestine or colon (column 3, lines 8-13). The cores are prepared either by granulation

or tableting and the tablets or cores that are coated are included in hard gelatin capsule dosage units (column 5, lines 9, 10, 27-35 and claim 1). Iamartino manufactures tablets using a tablet press (column 5, lines 57-59) and pressing in a tablet press produces compressed tablets. Regarding claim 22, although, Iamartino includes about 10 coated tablets or cores in a capsule (column5, lines 27-55), Iamartino nonetheless teaches the manufacture of tablet by tablet press and thus Iamartino's coated pressed tablet meets the scope of claim 22.

The active agents of Iamartino are 5-aminosalicylic acid (5-ASA) or corticoids for treating colonic and rectal disorders, antibacterial agents and antibiotics for treating local infectious diseases of the large intestine, anti-tumor chemotherapeutic agents for cancer therapy of the large intestine, cimetropium bromide antispasmodic drug, ketoprofen and ibuprofen non steroidal anti-inflammatory agents, and peptide or protein drugs (column 4, line 35 to column 5 line 2). Iamartino exemplifies the pharmaceutical preparation with ketoprofen (example 1), cimetropium bromide (example 2) and toluidine blue (example 3).

An inner coating layer in Iamartino comprises plasticizer and anionic copolymer EUDRAGIT S where the ratio of free carboxyl group to the ester group is 1:2 and the amount of the copolymer is in the range of 10-30% by weight gain on the core and it is suggested that a film thickness of 40-120 microns would ensure a quick dissolution of the coating layer at above pH 7.0 (column 3, lines 21-23 and lines 36-57).

An intermediate layer of gelling polymer (column 3, lines 24-26) comprises cellulose derivatives (column 3, lines 58-68). An outer layer of gastro-resistant polymer (column 3, lines 28-30) comprises common enteric material that are selected from cellulose acetate phthalate, hydroxypropylmethyl cellulose phthalate, polyvinyl acetate phthalate, hydroxyethyl cellulose

phthalate, cellulose acetate tetrahydrophthalate and EUDRAGIT L that dissolves at pH 5.5 (column 4, lines 21-29). The thickness of the outer layer in example 1 of Iamartino is listed as about 30 microns and the purpose of the outer layer is to enable the preparation to quickly dissolve in the intestine (column 3, lines 28-30).

The EUDRAGIT S of Iamartino is the poly(methacrylic acid, methyl methacrylate) 1:2 copolymer recited in instant claims 1-4 and 11-15. EUDRAGIT L is the poly(methacrylic acid, methyl methacrylate) 1:1 copolymer recited in instant claims 1-4 and 11-15. EUDRAGIT L, which is used in the outer layer differs from EUDRAGIT S of the inner layer. Instant claims 1 and 11 is a pharmaceutical composition that comprises a, b and c and the comprises language does not exclude the presence of the intermediate layer in Iamartino.

The teaching of Iamartino meets the limitations of the claims.

5. Claims 1-4, 8, 9, 11-14, 19, 20 and 22 remain rejected under 35 U.S.C. 102(b) as being anticipated by Rommelmayer (WO 98/27967, provided by applicants on form PTO 1449).

Applicants argue that the EUDRAGIT of Rommelmayer differs from that of the instant claims.

6. Applicants' arguments filed 07/14/03 have been fully considered but they are not persuasive. EUDRAGIT L is a combination of methacrylic and methylmethacrylate. The rejection is reiterated below.

Rommelmayer discloses a compressed tablet formulation for oral administration and the formulation comprises an inner core of biologically active ingredient and excipients, an enteric inner coating layer and an outer coating layer (page 1, lines 3-21 and page 18, lines 31 and 32). Among the biological agents disclosed by Rommelmayer are hydrocortisone, prednisone,

diclofenac sodium and piroxicam and ketoprofen and aspirin NSAIDs, codeine, morphine, antibiotics, antimicrobial agents, antihistamines, bronchodilators, antiemetics, antiviral drugs, anti-ulcer drugs, anti-Parkinson drugs, diuretics, calcium antagonists, anti-hypertension drugs, and drugs for treating cardiovascular diseases (page 12, line 17 to page 13 line 7). The inner coating comprises EUDRAGIT L 30D, which is sprayed onto the core (example 1), or phthalate (page 11, lines 4-14). The outer coating comprises EUDRAGIT RL 30D and EUDRAGIT RS 30D, which is also sprayed onto the cores (example 1) and the ratio of the RS and RL determines the release of the active agent (page 11, lines 29 and 30), on page 14, lines 17 and 18, Rommelmayer discloses that the outer coating layer can be either EUDRAGIT RL or a mixture of EUDRAGIT RS and EUDRAGIT RL and on page 11, lines 18-33, Rommelmayer discloses that the outer coating would consist of one or more polymers including EUDRAGIT copolymers. EUDRAGIT L in Rommelmayer is the poly(methacrylic acid, methyl methacrylate) 1:1 copolymer recited in instant claims 1-4 and 11-15. EUDRAGIT RL and EUDRAGIT RS are not the same as EUDRAGIT L (see page 11 of Rommelmayer). The comprising language of instant claims 1 and 11 does not exclude the presence of excipients and plasticizers. The teachings of Rommelmayer meet the limitations of the claims.

Claim Rejections - 35 USC § 103

Applicants argued against the rejection of claims 5-7 and 15-18 under 35 U.S.C. 103(a) over the prior art references of Iamartino and Rommelmayer. Applicants also argued against the rejection of claims 23 and 24 under 35 U.S.C. 103(b) or in the alternate under 35 U.S.C. 103(a) over the Iamartino and Rommelmayer references. The argument is basically the same as the

preceding arguments under Iamartino and Rommelmayer. The argument is not persuasive as stated in paragraphs 5 and 3. The rejections are reiterated below.

7. Claim 15 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rommelmayer (WO 98/27967).

Rommelmayer clearly teaches the orally administrable tablet of the instant invention by teaching an oral compressed tablet formulation that comprises a core of active agents, an inner coating layer comprising enteric coating materials selected from hydroxypropylmethylcellulose phthalate, polyvinyl acetate phthalate and acrylic and/or methacrylic acid/ester copolymers and EUDRAGIT L 30D and an outer coating layer comprising erodible polymer film selected from one or more polymers of ethylcellulose, polysiloxan, polyethylene and EUDRAGIT (page 11).

However, Rommelmayer while teaching an outer coating that comprises a mixture of EUDRAGIT RL 30D and EUDRAGIT RS 30D, does not teach an outer coating that is a mixture of poly (methacrylic acid, methyl methacrylate) 1:2 (EUDRAGIT S) and poly (methacrylic acid, methyl methacrylate) 1:1(EUDRAGIT L) as recited in instant claim 15. It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute a mixture of EUDRAGIT S and EUDRAGIT L for the mixture of EUDRAGIT RL 30D and EUDRAGIT RS 30D with the expectation that the tablet would release the active agent in the intestines. One having ordinary skill in the art would have been motivated to use the mixed EUDRAGIT co-polymers because Rommelmayer suggests that the use of mixture EUDRAGIT co-polymers in the outer coat layer determines the release of the active agent.

8. Claims 5-7 and 16-18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Iamartino et al. (US 5,171,580).

Claims 5-7 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Iamartino et al. (US 5,171,580, cited by applicants on form PTO 1449).

Iamartino clearly teaches the oral formulation of the instant invention by teaching tablets or cores of active agents that are coated by an inner layer comprising EUDRAGIT S (poly(methacrylic acid, methyl methacrylate) 1:2), an intermediate gelling polymer layer and outer layer comprising EUDRAGIT L (poly(methacrylic acid, methyl methacrylate) 1:1) and the tablets are included in a capsule such that the overall dosage form is a capsule (claim 1 and example 1).

Regarding instant claims 7 and 18 that recite the process of making the coated solid dosage form, although Iamartino teaches continuous spray coating of the tablets or cores with the coating layers, it is respectfully submitted that Iamartino teaches coated active cores or tablets and how the coated core is prepared is not critical in a formulation claim.

However, while Iamartino teaches inner layer coating and outer layer coating that has a thickness of from about 40 micron (inner layer) plus 30 micron (outer layer) to about 120 micron (inner layer) plus 30 micron (outer layer), that is, from about 70 micron to about 150 micron, Iamartino does not give the thickness of the coating layers in mg/cm^2. It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply to the cores or tablets an inner and outer coating layer of certain thickness since Iamartino teaches that the thickness of the coating layers determines the quick dissolution of the coating layer (column 3, lines 48 and 49). One having ordinary skill in the art would have been motivated to optimize the

thickness of the coating layer determined either in microns or mg/cm^2 with the expectation of producing desired quick dissolution of the coating layer.

9. Claims 23 and 24 remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rommelmayer (WO 98/27967).

Rommelmayer discloses the orally administrable tablet of the invention because Rommelmayer teaches the coated dosage forms of instant claims 1 and 11 for oral administration. Since the compressed tablet of Rommelmayer is orally administrable and the coating layers determine the release of active agents in the intestines, the teaching of Rommelmayer encompasses the scope of claims 23 and 24. Alternatively, one would be motivated to orally administer the coated tablet of Rommelmayer to the gastrointestinal tract because the method is explicit in Rommelmayer and the coated tablet of Rommelmayer is for oral administration.

10. Claims 23 and 24 remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Iamartino et al. (US 5,171,580).

Iamartino discloses the orally administrable formulation of claims 1 and 11 where the coating layer determines the release of active agents in the intestines. Thus the teaching of Iamartino encompasses the scope of claims 23 and 24. In the alternate, the method of administering the formulation of claims 1 and 11 to the gastrointestinal tract is explicit in Iamartino because the formulation of Iamartino, which anticipates claims 1 and 11 is orally administrable and therefore one would be motivated to orally administer the formulation of Iamartino to the gastrointestinal tract.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is 703-308-8374. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Blessing Fubara
Patent Examiner
Tech. Center 1600

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600